EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	63168	casein	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 10:39
L2	1291	L1 and (tyrosin$ near5 leucin$)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 10:41
L3	355	L2 and ($hypertension)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 10:41
L4	96	L2 and (angiotensin)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:13
L5	69	L2 and (ACE)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:08
L6	18	L2 and (trypsin near5 hydroly$)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 10:52
L7	58	L3 and L4	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:28
L8	27	L3 and L5	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 10:49
L9	2	L3 and L6	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 10:49
L10	3424	L1 and hypertension	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:29
L11	0	L1 and (trypsin near5 hydryoly$)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:29

EAST Search History

L12	6207	L1 and (trypsin)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:30
L13	17763	L1 and (hydrolys$)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:30
L14	13945	L1 and (hydrolyz$)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:31
L15	3098	L12 and L13	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:31
L16	2430	L12 and L14	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:31
L17	467	L15 and angiotensin	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:31
L18	431	L16 and angiotensin	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:32
L19	154	L17 and @pd<="20030624"	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:33
L20	135	L18 and @pd<="20030624"	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:33
L21	117	L19 and (converting adj enzyme)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:33
L22	116	L20 and (converting adj enzyme)	US-PGPUB; USPAT; USOCR; DERWENT	OR	ON	2006/11/16 11:34
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=> s angiotensin
L1 237648 ANGIOTENSIN

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L2 332 L1 AND CASEIN

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L3 14 L1 AND VENOM PEPTIDE

=> s L1 and peptide venom
L4 0 L1 AND PEPTIDE VENOM

=> s L2 and L3
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L3 ANSWER 1 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:203047 BIOSIS
DOCUMENT NUMBER: PREV199900203047
TITLE: Enhancement of bradykinin and resensitization of its B2 receptor.
AUTHOR(S): Marcic, Branislav; Deddish, Peter A.; Jackman, Herbert L.; Erdos, Ervin G. [Reprint author]
CORPORATE SOURCE: Department of Pharmacology (M/C 868), University of Illinois-Chicago, 835 S Wolcott Ave, Chicago, IL, 60612, USA
SOURCE: Hypertension (Baltimore), (March, 1999) Vol. 33, No. 3, pp. 835-843. print.
CODEN: HPRTDN. ISSN: 0194-911X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 1999
Last Updated on STN: 26 May 1999

AB We studied the enhancement of the effects of bradykinin B2 receptor agonists by agents that react with active centers of angiotensin -converting enzyme (ACE) independent of enzymatic inactivation. The potentiation and the desensitization and resensitization of B2 receptor were assessed by measuring (3H)arachidonic acid release and (Ca2+)i mobilization in Chinese hamster ovary cells transfected to express human ACE and B2 receptor, or in endothelial cells with constitutively expressed ACE and receptor. Administration of bradykinin or its ACE-resistant analogue desensitized the receptor, but it was resensitized (arachidonic acid release or (Ca2+)i mobilization) by agents such as enalaprilat (1 mumol/L). Enalaprilat was inactive in the absence of ACE expression. La3+ (100 mumol/L) inhibited the apparent resensitization, probably by blocking the entry of extracellular calcium. Enalaprilat resensitized the receptor via ACE to release arachidonic acid by bradykinin at a lower concentration (5 nmol/L) than required to mobilize (Ca2+)i (1 mumol/L).

Monoclonal antibodies inhibiting the ACE N-domain active center and polyclonal antiserum potentiated bradykinin. The snake venom peptide BPP5a and metabolites of angiotensin and bradykinin (angiotensin-(1-9), angiotensin-(1-7), bradykinin-(1-8); 1 mumol/L) enhanced arachidonic acid release by bradykinin. Angiotensin-(1-9) and -(1-7) also resensitized the receptor. Enalaprilat potentiated the bradykinin effect in cells expressing a mutant ACE with a single N-domain active site. Agents that reacted with a single active site, on the N-domain or on the C-domain, potentiated bradykinin not by blocking its inactivation but by inducing crosstalk between ACE and the receptor. Enalaprilat enhanced signaling via ACE by Galphai in lower concentration than by Galphaq-coupled receptor.

L3 ANSWER 2 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:265112 BIOSIS
DOCUMENT NUMBER: PREV199800265112
TITLE: Isolation: Analysis and properties of three bradykinin-potentiating peptides (BPP-II, BPP-III, and BPP-V) from Bothrops neuwiedi venom.
AUTHOR(S): Faria-Ferreira, L. A. [Reprint author]; Galle, A.; Raida, M.; Schrader, M.; Lebrun, I.; Habermehl, G.
CORPORATE SOURCE: Lab. Bioquim. e Biofisica Inst. Butantan, Vital Brasil 1500, Cep. 05503-900 Sao Paulo, SP, Brazil
SOURCE: Journal of Protein Chemistry, (April, 1998) Vol. 17, No. 3, pp. 285-289. print.
CODEN: JPCHD2. ISSN: 0277-8033.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 1998
Last Updated on STN: 12 Aug 1998
AB In the course of systematic investigations on low-molecular-weight compounds from the venom of Crotalidae and Viperidae, we have isolated and characterized at least three bradykinin-potentiating peptides (BPP-II, BPP-III, and BPP-V) from Bothrops neuwiedi venom by gel filtration on Sephadex G-25 M, Sephadex G-10 followed by HPLC. The peptides showed bradykinin-potentiating action on isolated guinea-pig ileum, for which the BPP-V was more active than of BPP-II, and BPP-III, rat arterial blood pressure, and a relevant angiotensin-converting enzyme (ACE) competitive inhibiting activity. The kinetic studies showed a Ki of the order of 9.7 X 10-3 muM to BPP-II, 7 X 10-3 muM to BPP-III, and 3.3 X 10-3 muM to BPP-V. The amino acid sequence of the BPP-III has been determined to be pGlu-Gly-Gly-Trp-Pro-Arg-Pro-Gly-Pro-Glu-Ile-Pro-Pro, and the amino acid compositions of the BPP-II and BPP-V by amino acid analysis were 2Glu-2Gly-1Arg-4Pro-1Ile and 2Glu-2Gly-1Ser-3Pro-2Val-Ille, with molecular weight of 1372, 1046, and 1078, respectively.

L3 ANSWER 3 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:385110 BIOSIS
DOCUMENT NUMBER: PREV199396060410
TITLE: Mechanism of mastoparan-induced EDRF release from pulmonary artery endothelial cells.
AUTHOR(S): Tracey, W. Ross [Reprint author]; Peach, Michael J.
CORPORATE SOURCE: Dep. 46B, Bldg. AP10/2, Abbott Lab., One Abbott Park Road, Abbott Park, IL 60064-3500, USA
SOURCE: Journal of Vascular Research, (1993) Vol. 30, No. 2, pp. 68-72.
CODEN: JVREE9. ISSN: 1018-1172.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 1993
Last Updated on STN: 3 Jan 1995
AB Mastoparan is a wasp venom peptide that activates G-proteins, certain classes of which are involved in the release of

endothelium-derived relaxing factor (EDRF). In the present study, we investigated whether this peptide might be a useful tool with which to elucidate the signal transduction pathways responsible for EDRF release from pulmonary artery endothelium. Mastoparan (10-50 mu-g/ml) elicited an increase in endothelial cell cytosolic free calcium concentration ((Ca-2+)-i) and EDRF release in a concentration-dependent manner. Both effects were dependent on Ca-2+ influx, as they were inhibited by removal of extracellular Ca-2+. In addition, when endothelial cells were suspended in Ca-2+-free buffer, mastoparan inhibited ATP-induced increases in (Ca-2+)-i, presumably by depleting intracellular Ca-2+ stores. More importantly, mastoparan also caused the release of fura-2 from dye-loaded endothelial cells, unlike ATP, which did not affect fura-2 loss. These data indicate that although mastoparan may act on G-proteins to elicit release of Ca-2+ from intracellular stores, the primary mechanism of action responsible for mastoparan's ability to elicit EDRF release is an increase in cell membrane permeability followed by an influx of extracellular Ca-2+.

L3 ANSWER 4 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:207646 BIOSIS
DOCUMENT NUMBER: PREV199191110871; BA91:110871
TITLE: PRODUCTION OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS FROM BAKER'S YEAST GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE.
AUTHOR(S): KOHAMA Y [Reprint author]; NAGASE Y; OKA H; NAKAGAWA T; TERAMOTO T; MURAYAMA N; TSUJIBO H; INAMORI Y; MIMURA T
CORPORATE SOURCE: FAC PHARM SCI, OSAKA UNIV, YAMADAOKA 1-6, SUITA, OSAKA 565, JPN
SOURCE: Journal of Pharmacobio-Dynamics, (1990) Vol. 13, No. 12, pp. 766-771.
CODEN: JOPHDQ. ISSN: 0386-846X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 2 May 1991
Last Updated on STN: 3 May 1991

AB Angiotensin-coverting enzyme (ACE) inhibitors were excised from the molecule of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) preparation of baker's yeast by heating at 120° C in 1 M AcOH-20 mM HCl. Three inhibitors were then purified by gel-permeation and reverse-phase chromatographies. One of the yeast ACE inhibitors, YG-3, was GAPDH peptide 79-89 (Pro-Ala-Asn-Leu-Pro-Trp-Gly-Ser-Ser-Asn-Val, IC50: 18 μm), and contained the sequence homologous to vertebrate ACE inhibitors (GAPDH peptides 79-86 or 81-88). Other inhibitors, YG-1 (Gly-His-Lys-Ile-Ala-Thr-Phe-Gln-Glu-Arg, IC50: 0.4 μM) and YG-2 (Gly-Lys-Lys-Ile-Ala-Thr-Tyr-Gln-Glu-Arg, IC50: 2 μM), correspond to amino acid residues 68-77 in two different forms of yeast GAPDH, respectively. Their sequences were quite different from those of the venom peptide family. YG-1 was the most potent ACE inhibitor among yeast and vertebrate GAPDH peptides excised by acid-limited proteolysis. Thus, yeast GAPDH seems to be an excellent source of naturally occurring ACE inhibitors.

L3 ANSWER 5 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:3405 BIOSIS
DOCUMENT NUMBER: PREV199191003405; BA91:3405
TITLE: BACILLUS-STEAROTHERMOPHILUS GLYCERALDEHYDE-3-PHOSPHATE DEHYDROGENASE AS A SOURCE OF ANGIOTENSIN -CONVERTING ENZYME INHIBITORS.
AUTHOR(S): KOHAMA Y [Reprint author]; NAKAGAWA T; OKA H; OKUNO Y; MIMURA T; TSUJIBO H; INAMORI Y; TSURUTANI R; NAGATA K; TOMITA K
CORPORATE SOURCE: FAC OF PHARMACEUTICAL SCI, OSAKA UNIV, YAMADAOKA 1-6, SUITA, OSAKA 565, JAPAN

SOURCE: Agricultural and Biological Chemistry, (1990) Vol. 54, No. 8, pp. 2115-2120.
CODEN: ABCHA6. ISSN: 0002-1369.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 8 Dec 1990
Last Updated on STN: 9 Dec 1990

AB The more potent inhibitory activity against angiotensin -converting enzyme (ACE) was excised from a glyceraldehyde-3-phosphate dehydrogenase (GAPDH) preparation of Bacillus stearothermophilus by heating at 120° C in 1 M AcOH-20 mM HC1, as compared with GAPDH preparations of yeast and pig. Sufficient excision of B. stearothermophilus ACE inhibitors required a longer proteolysis time of 60 min. Two inhibitors were then purified by gel-permeation and reverse-phase chromatographies. One of the B. stearothermophilus ACE inhibitors, BG-1, was the GAPDH peptide 68-77 (Gly-Lys-Glu-Ile-Ile-Val-Lys-Ala-Glu-Arg, IC50: 32 μM). Another inhibitor, BG-2 (Gly-Lys-Met-Val-Lys-Val-Val-Ser-Trp-Tyr, IC50: 6 μM), corresponded to GAPDH peptide 304-313. These sequences were quite different from those of vertebrate GAPDH peptides and the venom peptide family with ACE inhibitory activity. BG-2 was found to be a non-competitive type inhibitor, differing from many natural peptide inhibitors. Thus, B. stearothermophilus GAPDH seemed to be a good source of new type ACE inhibitors, in addition to the advantages due to its thermophilic property.

L3 ANSWER 6 OF 14 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1989:46466 BIOSIS
DOCUMENT NUMBER: PREV198936023783; BR36:23783
TITLE: EVOLUTION OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS.
AUTHOR(S): WYVRATT M J [Reprint author]
CORPORATE SOURCE: MERCK SHARP AND DOHME RES LAB, RAHWAY, NJ 07065, USA
SOURCE: Clinical Physiology and Biochemistry, (1988) Vol. 6, No. 3-4, pp. 217-229.
Meeting Info.: SYMPOSIUM ON THE BIOCHEMISTRY OF HYPERTENSION HELD AT THE 11TH ANNUAL MEETING OF THE NATIONAL ACADEMY OF CLINICAL BIOCHEMISTRY, SAN FRANCISCO, CALIFORNIA, USA, JULY 17-18, 1987. CLIN PHYSIOL BIOCHEM.
CODEN: CPBIDP. ISSN: 0252-1164.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 27 Dec 1988
Last Updated on STN: 27 Dec 1988

L3 ANSWER 7 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1999107753 EMBASE
TITLE: Enhancement of bradykinin and resensitization of its B2 receptor.
AUTHOR: Marcic B.; Deddish P.A.; Jackman H.L.; Erdos E.G.
CORPORATE SOURCE: Dr. E.G. Erdos, Department of Pharmacology, M/C 868, University of Illinois-Chicago, 835 S Wolcott Ave, Chicago, IL 60612, United States. EGErdos@uic.edu
SOURCE: Hypertension, (1999) Vol. 33, No. 3, pp. 835-843. .
Refs: 57
ISSN: 0194-911X CODEN: HPRTDN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Apr 1999
Last Updated on STN: 28 Apr 1999

AB We studied the enhancement of the effects of bradykinin B2 receptor agonists by agents that react with active centers of angiotensin -converting enzyme (ACE) independent of enzymatic inactivation. The potentiation and the desensitization and resensitization of B2 receptor were assessed by measuring [3H]arachidonic acid release and [Ca2+](i) mobilization in Chinese hamster ovary cells transfected to express human ACE and B2 receptor, or in endothelial cells with constitutively expressed ACE and receptor. Administration of bradykinin or its ACE-resistant analogue desensitized the receptor, but it was resensitized (arachidonic acid release or [Ca2+](i) mobilization) by agents such as enalaprilat (1 μmol/L). Enalaprilat was inactive in the absence of ACE expression. La3+ (100/μmol/L) inhibited the apparent resensitization, probably by blocking the entry of extracellular calcium. Enalaprilat resensitized the receptor via ACE to release arachidonic acid by bradykinin at a lower concentration (5 nmol/L) than required to mobilize [Ca2+](i) (1 μmol/L). Monoclonal antibodies inhibiting the ACE N-domain active center and polyclonal antiserum potentiated bradykinin. The snake venom peptide BPP5a and metabolites of angiotensin and bradykinln :(angiotensin-[1-9], angiotensin-[1-7], bradykinin-[1-8]; 1 μmol/L) enhanced arachidonic acid release by bradykinin. Angiotensin (1-9) and -(1,7) also resensitized the receptor. Enalaprilat potentiated the bradykinin effect in cells expressing a mutant ACE with a single N-domain active site. Agents that reacted with a single active site, on the N-domain or on the C-domain, potentiated bradykinin not by blocking its inactivation but by inducing crosstalk between ACE and the receptor. Enalaprilat enhanced signaling via ACE by Gα(i) in lower concentration than by Gα(q)-coupled receptor.

L3 ANSWER 8 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 82208347 EMBASE
DOCUMENT NUMBER: 1982208347
TITLE: Development and design of specific inhibitors of angiotensin-converting enzyme.
AUTHOR: Cushman D.W.; Cheung H.S.; Sabo E.F.; Ondetti M.A.
CORPORATE SOURCE: Squibb Inst. Med. Res., Princeton, NJ 08540, United States
SOURCE: American Journal of Cardiology, (1982) Vol. 49, No. 6, pp. 1390-1394. .
CODEN: AJCDAG
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB Captopril is a remarkably effective new antihypertensive drug designed and developed as a potent and specific inhibitor of angiotensin -converting enzyme, a zinc metallopeptidase that participates in the synthesis of a hypertensive peptide, angiotensin II, and in the degradation of a hypotensive peptide, bradykinin. Earlier studies with a snake venom peptide (teprotride or SQ 20881) that could be administered only by injection demonstrated that specific inhibitors of angiotensin-converting enzyme could be highly effective as antihypertensive drugs, and helped to clarify the specificity and mechanim of action of the enzyme. A hypothetical model of the active center of angiotensin-converting enzyme based on its presumed analogy to the well characterized zinc metallopeptidase carboxypeptidase A was used to guide logical sequential improvements of a weakly active

prototype inhibitor that led eventually to the highly optimized structure of captopril. The hypothetical working model of the active site of angiotensin-converting enzyme used to develop captopril continues to provide a firm basis for development of new types of specific inhibitors of this biologically important enzyme.

L3 ANSWER 9 OF 14 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 80079370 EMBASE
DOCUMENT NUMBER: 1980079370
TITLE: Development of specific inhibitors of angiotensin I converting enzyme (kininase II).
AUTHOR: Cushman D.W.; Cheung H.S.; Sabo E.F.; et al.
CORPORATE SOURCE: Squibb Inst. Med. Res., Princeton, N.J. 08540, United States
SOURCE: Federation Proceedings, (1979) Vol. 38, No. 13, pp. 2778-2782. .
CODEN: FEPRA7
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB Angiotensin I converting enzyme, a zinc-containing dipeptide-releasing carboxypeptidase, may contribute to elevated blood pressure in hypertensive disease via conversion of angiotensin I to angiotensin II or inactivation or bradykinin. The first therapeutically useful inhibitor of this enzyme was a snake venom peptide SQ 20,881 or teprotide (<Glu-Trp-Pro-Arg-Pro-Gln-Ile-Pro-Pro). Studies with venom peptides and their structural analogs have helped to elucidate the specificity and catalytic mechanism of angiotensin I converting enzyme and to reveal its similarity to the well-characterized pancreatic carboxypeptidase A. Clinical studies with teprotide have demonstrated the potential of such converting enzyme inhibitors for use as antihypertensive drugs. Recently, a new series of potent and specific orally active inhibitors of angiotensin I converting enzyme has been developed using a hypothetical model of the active site of this enzyme, based on its presumed similarity to the known active site of carboxypeptidase A. The design of simple nonpeptidic compounds expected to have multifunctional interactions with this putative active site had led to increasingly more potent and specific inhibitors. Captopril or SQ 14,225 (D-3-mercapto-2-methylpropanoyl-L-proline) is an extremely potent competitive inhibitor (K(i)=1.7 nM) that appears to be of great value for use in chronic therapy of human hypertensive disease.

L3 ANSWER 10 OF 14 MEDLINE on STN

ACCESSION NUMBER: 1999182397 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10082496
TITLE: Enhancement of bradykinin and resensitization of its B2 receptor.
AUTHOR: Marcic B; Deddish P A; Jackman H L; Erdos E G
CORPORATE SOURCE: Departments of Pharmacology, University of Illinois College of Medicine at Chicago, 60612, USA.
CONTRACT NUMBER: HL-36473 (NHLBI)
HL-58118 (NHLBI)
SOURCE: Hypertension, (1999 Mar) Vol. 33, No. 3, pp. 835-43.
Journal code: 7906255. ISSN: 0194-911X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 26 Apr 1999
Last Updated on STN: 26 Apr 1999
Entered Medline: 13 Apr 1999

AB We studied the enhancement of the effects of bradykinin B2 receptor agonists by agents that react with active centers of angiotensin -converting enzyme (ACE) independent of enzymatic inactivation. The potentiation and the desensitization and resensitization of B2 receptor were assessed by measuring [3H]arachidonic acid release and [Ca2+]i mobilization in Chinese hamster ovary cells transfected to express human ACE and B2 receptor, or in endothelial cells with constitutively expressed ACE and receptor. Administration of bradykinin or its ACE-resistant analogue desensitized the receptor, but it was resensitized (arachidonic acid release or [Ca2+]i mobilization) by agents such as enalaprilat (1 micromol/L). Enalaprilat was inactive in the absence of ACE expression. La3+ (100 micromol/L) inhibited the apparent resensitization, probably by blocking the entry of extracellular calcium. Enalaprilat resensitized the receptor via ACE to release arachidonic acid by bradykinin at a lower concentration (5 nmol/L) than required to mobilize [Ca2+]i (1 micromol/L). Monoclonal antibodies inhibiting the ACE N-domain active center and polyclonal antiserum potentiated bradykinin. The snake venom peptide BPP5a and metabolites of angiotensin and bradykinin (angiotensin-[1-9], angiotensin-[1-7], bradykinin-[1-8]; 1 micromol/L) enhanced arachidonic acid release by bradykinin. Angiotensin-(1-9) and -(1-7) also resensitized the receptor. Enalaprilat potentiated the bradykinin effect in cells expressing a mutant ACE with a single N-domain active site. Agents that reacted with a single active site, on the N-domain or on the C-domain, potentiated bradykinin not by blocking its inactivation but by inducing crosstalk between ACE and the receptor. Enalaprilat enhanced signaling via ACE by Galphai in lower concentration than by Galphaq-coupled receptor.

L3 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 91277921 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2098549
TITLE: Production of angiotensin-converting enzyme inhibitors from baker's yeast glyceraldehyde-3-phosphate dehydrogenase.
AUTHOR: Kohama Y; Nagase Y; Oka H; Nakagawa T; Teramoto T; Murayama N; Tsujibo H; Inamori Y; Mimura T
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Osaka University, Japan.
SOURCE: Journal of pharmacobio-dynamics, (1990 Dec) Vol. 13, No. 12, pp. 766-71.
Journal code: 7901854. ISSN: 0386-846X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 18 Aug 1991
Last Updated on STN: 29 Jan 1999
Entered Medline: 1 Aug 1991

AB Angiotensin-converting enzyme (ACE) inhibitors were excised from the molecule of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) preparation of baker's yeast by heating at 120 degrees C in 1 M AcOH-20 mM HCl. Three inhibitors were then purified by gel-permeation and reverse-phase chromatographies. One of the yeast ACE inhibitors, YG-3, was GAPDH peptide 79-89 (Pro-Ala-Asn-Leu-Pro-Trp-Gly-Ser-Ser-Asn-Val, IC50:18 microM), and contained the sequence homologous to vertebrate ACE inhibitors (GAPDH peptides 79-86 or 81-88). Other inhibitors, YG-1 (Gly-His-Lys-Ile-Ala-Thr-Phe-Gln-Glu-Arg, IC50: 0.4 microM) and YG-2

(Gly-Lys-Lys-Ile-Ala-Thr-Tyr-Gln-Glu-Arg, IC50: 2 microM), corresponded to amino acid residues 68-77 in two different forms of yeast GAPDH, respectively. Their sequences were quite different from those of the venom peptide family. YG-1 was the most potent ACE inhibitor among yeast and vertebrate GAPDH peptides excised by acid-limited proteolysis. Thus, yeast GAPDH seems to be an excellent source of naturally occurring ACE inhibitors.

L3 ANSWER 12 OF 14 MEDLINE on STN
ACCESSION NUMBER: 91182410 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1368612
TITLE: Bacillus stearothermophilus glyceraldehyde-3-phosphate dehydrogenase as a source of angiotensin -converting enzyme inhibitors.
AUTHOR: Kohama Y; Nakagawa T; Oka H; Okuno Y; Mimura T; Tsujibo H; Inamori Y; Tsurutani R; Nagata K; Tomita K
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Osaka University, Japan.
SOURCE: Agricultural and biological chemistry, (1990 Aug) Vol. 54, No. 8, pp. 2115-9.
Journal code: 0370452. ISSN: 0002-1369.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Biotechnology
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 9 Aug 1995
Last Updated on STN: 29 Jan 1999
Entered Medline: 8 May 1991

AB The more potent inhibitory activity against angiotensin -converting enzyme (ACE) was excised from a glyceraldehyde-3-phosphate dehydrogenase (GAPDH) preparation of Bacillus stearothermophilus by heating at 120 degrees C in 1 M AcOH-20 mM HCl, as compared with GAPDH preparations of yeast and pig. Sufficient excision of B. stearothermophilus ACE inhibitors required a longer proteolysis time of 60 min. Two inhibitors were then purified by gel-permeation and reverse-phase chromatographies. One of the B. stearothermophilus ACE inhibitors BG-1, was the GAPDH peptide 68-77 (Gly-Lys-Glu-Ile-Ile-Val-Lys-Ala-Glu-Arg, IC50: 32 microM). Another inhibitor, BG-2 (Gly-Lys-Met-Val-Lys-Val-Val-Ser-Trp-Tyr, IC50: 6 microM), correspond to GAPDH peptide 304-313. These sequences were quite different from those of vertebrate GAPDH peptides and the venom peptide family with ACE inhibitory activity. BG-2 was found to be a non-competitive type inhibitor, differing from many natural peptide inhibitors. Thus, B. stearothermophilus GAPDH seemed to be a good source of new type ACE inhibitors, in addition to the advantages due to its thermophilic property.

L3 ANSWER 13 OF 14 MEDLINE on STN
ACCESSION NUMBER: 89077785 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2849521
TITLE: Evolution of angiotensin-converting enzyme inhibitors.
AUTHOR: Wyvratt M J
CORPORATE SOURCE: Merck Sharp & Dohme Research Laboratories, Rahway, N.J.
SOURCE: Clinical physiology and biochemistry, (1988) Vol. 6, No. 3-4, pp. 217-29. Ref: 40
Journal code: 8305885. ISSN: 0252-1164.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 9 Feb 1989

AB The renin-angiotensin system is perhaps the most important hormonal system in the regulation of blood pressure. Its influence on blood pressure is mediated by the potent vasoconstrictor angiotensin II. Since angiotensin-converting enzyme performs the last step in the biosynthesis of angiotensin II, inhibition of this enzyme has attracted the attention of many researchers as a novel approach in the control of high blood pressure. The evolution of inhibitors of this enzyme will be traced from the early snake venom peptide inhibitors to the drugs currently available for the treatment of high blood pressure and congestive heart failure.

L3 ANSWER 14 OF 14 MEDLINE on STN
ACCESSION NUMBER: 82179297 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6176105
TITLE: Development and design of specific inhibitors of angiotensin-converting enzyme.
AUTHOR: Cushman D W; Cheung H S; Sabo E F; Ondetti M A
SOURCE: The American journal of cardiology, (1982 Apr 21) Vol. 49, No. 6, pp. 1390-4.
Journal code: 0207277. ISSN: 0002-9149.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198206
ENTRY DATE: Entered STN: 17 Mar 1990
Last Updated on STN: 17 Mar 1990
Entered Medline: 24 Jun 1982

AB Captopril is a remarkably effective new antihypertensive drug designed and developed as a potent and specific inhibitor of angiotensin -converting enzyme, a zinc metallopeptidase that participates in the synthesis of a hypertensive peptide, angiotensin II, and in the degradation of a hypotensive peptide, bradykinin. Earlier studies with a snake venom peptide (teprotride or SQ 20881) that could be administered only by injection demonstrated that specific inhibitors of angiotensin-converting enzyme could be highly effective as antihypertensive drugs, and helped to clarify the specificity and mechanism of action of the enzyme. A hypothetical model of the active center of angiotensin-converting enzyme based on its presumed analogy to the well characterized zinc metallopeptidase carboxypeptidase A was used to guide logical sequential improvements of a weakly active prototype inhibitor that led eventually to the highly optimized structure of captopril. The hypothetical working model of the active site of angiotensin-converting enzyme used to develop captopril continues to provide a firm basis for development of new types of specific inhibitors of this biologically important enzyme.